PATENT COOPERATION TREATY

From the:
INTERNATIONAL SEARCHING AUTHORITY

To:

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BALMAIN NSW 2041

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	08 SEP 2004
Applicant's or agent's file reference 119149/ROB/car	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/AU2004/000788	17 June 2004	17 June 2003

International Patent Classification (IPC) or both national classification and IPC
Int. Cl. [7] A61K 38/39; A61P 19/02

Applicant
INSTITUTE OF NUTRACEUTICAL RESEARCH PTY LTD et al

1. This opinion contains indications relating to the following items:

- [X] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [X] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [ ] Box No. VIII — Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU	Authorized Officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	JASON MACKENZIE Telephone No. (02) 6283 7934

WRITTEN OPINION OF THE
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International application No.
PCT/AU2004/000788

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing
      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format
      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in the international application as filed.
      ☐ filed together with the international application in computer readable form.
      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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International application No.
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Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	19-20	YES
	Claims	1-18, 21-28	NO
Inventive step (IS)	Claims	19-20	YES
	Claims	1-18, 21-28	NO
Industrial applicability (IA)	Claims	1-28	YES
	Claims		NO

2. Citations and explanations:

D1 US 5925736 (Neff et al., 20 July 1999).
D2 WO 2001/093833 (The Procter & Gamble Company, 13 December 2001).
D3 WO 2001/093831 (The Procter & Gamble Company, 13 December 2001).
D5 Myers et al.
D6 Vasios et al.
D7 Lu et al.

Novelty (N) claims 1-18, 21-28

Independent claim 1 defines a composition comprising a polypeptide, which further comprises a collagen type IX alpha 1 chain NC4 domain or biologically active fragment thereof having antiarthritic or antiinflammatory activity, and a suitable carrier, for use in treating/preventing arthritis or other degenerative diseases. Please note that in Australia, "composition for use" type claims are considered to claim the composition per se.

Independent claim 2 defines a similar composition to that of claim 1, for inducing tolerance to at least one antigenic component of cartilage in an individual.

Independent claims 12 and 16, respectively, claims methods of inducing tolerance to at least one antigenic component of cartilage, and of preventing a musculoskeletal degenerative condition in an individual, using compositions similar to those of claims 1 and 2. Independent claims 27 and 28 are similar in scope to claims 12 and 16, but are drafted as Swiss-type method of treatment claims.

Independent claims 19 and 20 define methods of preparing antiarthritic or antiinflammatory polypeptides, which are isolated from connective tissue that is subjected to autolysis, have a MW of about 30 kDa, and which are free of glycosaminoglycans.

Independent claims 21 and 23, respectively, claim polypeptides and compositions comprising polypeptides obtainable by methods similar to claims 19 and 20. Please note that "obtainable" does not necessarily restrict the polypeptides of claims 21 and 23 to only those which are isolated according to only those methods.

D1 discloses the administration of collagen type IX (which would include the alpha 1 chain NC4 domain) in a method of treating arthritis, and in a method of inducing tolerance to an antigenic component of cartilage (see the whole document, particularly column 2 lines 1-58, column 4 lines 45-53, column 7 lines 17-67, Table I, column 9 line 32 – column 10 line 34, and claims 1-9). Therefore claims 1-18 and 21-28 are considered to be deprived of novelty. The document does not disclose a method as defined in claims 19-20.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: box V

Novelty (N) claims 1-18, 21-28 (continued)

D2 discloses the use of cartilage (bovine or shark) which are reasonably expected to contain the collagen type IX alpha 1 chain NC4 domain, in a method of treating arthritis (See the whole document, particularly the abstract, summary of the invention, page 6 under the heading "Cartilage", and claims 1-2.) Therefore claims 1-11, 16-18, and 21-27 are considered to be deprived of novelty. The document does not disclose a method as defined in claims 19-20, nor the methods of claims 12-15 and 28.

D3 discloses the use of cartilage (bovine or shark) which are reasonably expected to contain the collagen type IX alpha 1 chain NC4 domain, in a method of treating arthritis (See the whole document, particularly the abstract, summary of the invention, pages 8-9 under the heading "Cartilage", and claims 1-3.) Therefore claims 1-11, 16-18, and 21-27 are considered to be deprived of novelty. The document does not disclose a method as defined in claims 19-20, nor the methods of claims 12-15 and 28.

D5 (identified in the current application) and the references therein (see specifically reference 12 of D5) discloses the use of recombinant human collagen type IX alpha sequences (1-3) in a method of inducing tolerance in an animal model of collagen induced arthritis (see the whole document). The compositions disclosed therein can be reasonably expected to include the type IX alpha 1 chain NC4 domain, as they were produced using primers for the 5' and 3' noncoding sequences of the type IX alpha 1 chain cDNA. Therefore claims 1-18 and 21-28 are considered to be deprived of novelty. The document does not disclose a method as defined in claims 19-20.

D6 (identified in the current application) describes the isolation and characterisation of the NC4 (amino terminal noncollagenous domain) of type IX collagen (see the whole document). Therefore claims 1-11, and 21-26 are considered to be deprived of novelty. The document does not disclose a method as defined in claims 12, 16, 19-20, 27 or 28.

D7 (identified in the current application) discloses the therapeutic administration of rat collagen type IX in an animal model of pristine induced arthritis (see the whole document, particularly the results on page 121). Therefore claims 1-18 and 21-28 are considered to be deprived of novelty. The document does not disclose a method as defined in claims 19-20.

Inventive Step (IS) claims 1-18, 21-28

Claims 1-18 and 21-28 are already found wanting of novelty as above, and therefore are also deprived of an inventive step.

Industrial Applicability (IA)

All of claims 1-28 appear to be industrially applicable

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International application No.
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Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 2003/062279 A1	31 July 2003	23 January 2003	23 January 2002

WO 2003/062279 (D4) is published after the priority date of the current application, but enjoys an earlier priority date. This document discloses autolysis of connective tissues and the isolation of glycosaminoglycan-peptide complexes as well as polypeptides per se. D4 is silent to the isolation and use of polypeptides comprising collagen type IX alpha 1 chain NC4 domain, and the antiarthritic/antiinflammatory polypeptides isolated following autolysis are larger than 30 kDa (see Table 2 on page 42). Therefore D4 is not considered to be relevant to the patentability of any of the current claims.

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*